Overview of the New Content and Format Requirements for Prescription Drug Labeling

Background

- Previous labeling regulations finalized in 1979
- Increase in amount and complexity of drug information
- Goal - more informative and accessible labeling, resulting in a better risk communication and management tool
- Development process included
  - Focus groups
  - National physician survey
  - Public meeting
  - Written comments
- Proposed rule issued December 2000
- Final rule published January 24, 2006

Content Innovations

- *Highlights*
  - Limited to ½ page
  - Bulleted Boxed Warning and Indications
- *Table of Contents ("Contents")*
  - Allows easy reference to full prescribing information (FPI)
  - Facilitates hyperlinks in electronic formats
- Identifies and Dates "Recent Major Changes"
  - Captures *Indications, D&A, Boxed Warning, CI and W&P*
  - Referenced in *Highlights*; margin mark in FPI
- Added date of initial US approval

Format Innovations

- Reorders and reorganizes sections
  - Frequently referenced information moved forward
  - Safety information consolidated
- Establishes format requirements
  - Minimum 8-point font (note minimum 6-point font trade labeling that accompanies drug product)
  - Standardizes bolding and “white space”

Other Format Changes

- *Warnings and Precautions* consolidated
- Formerly in Precautions, now new sections
  - *Drug Interactions*
  - *Use in Specific Populations*
  - *Patient Counseling Information*
- Formerly optional, now required
  - *Clinical Studies*
  - *Nonclinical Toxicology*
- Created *Dosage Forms and Strengths* and moved *How Supplied* to near end

Other Improvements

- Emphasizes "*Patient Counseling Information*"
  - Referenced in Highlights
  - New section in FPI
  - Approved patient labeling, if available, is reprinted at end
- Adds the established pharmacologic class to Highlights
- Encourages AR reporting by including contact information (toll-free number and internet address)
- Added an explicit requirement to update labeling
- Provides greater clarity in requirements

Highlights

- Limitations Statement
- Product Names and Date of Initial US Approval
- Boxed Warning
- Major Recent Changes
- Indications and Usage
- Dosage & Administration
- Dosage Forms & Strengths
- Contraindications
- Warnings & Precautions
- Adverse Reactions
- Drug Interactions
- Use in Specific Populations
- Patient Counseling Information Statement

Contents and Full Prescribing Information (FPI)

- Boxed Warning
- 1 Indications & Usage
- 2 Dosage & Administration
- 3 Dosage Forms & Strengths
- 4 Contraindications
- 5 Warnings & Precautions
- 6 Adverse Reactions
- 7 Drug Interactions
- 8 Use in Specific Populations
- 9 Drug Abuse & Dependence
- 10 Overdosage
- 11 Description
- 12 Clinical Pharmacology
- 13 Nonclinical Toxicology
- 14 Clinical Studies
- 15 References
- 16 How Supplied/Storage & Handling
- 17 Patient Counseling Information

Example of Highlights for a Fictitious Drug

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

IMDICON® (cholinasol) CAPSULES
Initial U.S. Approval: 2000

WARNING: LIFE-THREATENING HEMATOLOGICAL ADVERSE REACTIONS
***See full prescribing information for complete boxed warning*.**
Monitor for hematological adverse reactions every 2 weeks for first 3 months of treatment (5.2). Discontinue Imdicon immediately if any of the following occur:
- **Neutropenia/agranulocytosis (5.1)**
- **Thrombotic thrombocytopenic purpura (5.1)**
- **Aplastic anemia (5.1)**

----------RECENT MAJOR CHANGES----------

Indications and Usage, Coronary Stenting (1.2)	2/200X
Dosage and Administration, Coronary Stenting (2.2)	2/200X

----------INDICATIONS AND USAGE----------
Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:
- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:
- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

----------DOSAGE AND ADMINISTRATION----------
- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

----------DOSAGE FORMS AND STRENGTHS----------
Capsules: 50 mg (3)

----------CONTRAINDICATIONS----------
- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)
- Severe hepatic impairment (4, 8.7)

----------WARNINGS AND PRECAUTIONS----------
- Neutropenia (2.4 % incidence; may occur suddenly; typically resolves within 1-2 weeks of discontinuation), thrombotic thrombocytopenic purpura (TTP), aplastic anemia, agranulocytosis, pancytopenia, leukemia, and thrombocytopenia can occur (5.1)
- Monitor for hematological adverse reactions every 2 weeks through the third month of treatment (5.2)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence >2%) are diarrhea, nausea, dyspepsia, rash, gastrointestinal pain, neutropenia, and purpura (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------DRUG INTERACTIONS----------
- Anticoagulants: Discontinue prior to switching to Imdicon (5.3, 7.1)
- Phenytoin: Elevated phenytoin levels have been reported. Monitor levels. (7.2)

----------USE IN SPECIFIC POPULATIONS----------
- Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
- Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 5/200X

Example of Contents for a Fictitious Drug

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

Implementation Schedule

New NDA/BLA or efficacy supplement submitted:	Label must conform:
6/30/06 or after	At time of submission
Pending on 6/30/06 Approved 6/30/05-6/30/06	6/30/09 (3 years)
Approved 6/30/04-6/29/05	6/30/10 (4 years)
Approved 6/30/03-6/29/04	6/30/11 (5 years)
Approved 6/30/02-6/29/03	6/30/12 (6 years)
Approved 6/30/01-6/29/02	6/30/13 (7 years)
Approved Pre-6/30/01	Voluntary at any time (encouraged to conform)

Resources on FDA's Website

Dedicated Web page

http://www.fda.gov/cder/regulatory/physLabel/default.htm

- Final rule
- Guidance for Industry
  - Implementing the new labeling content and format (draft)
  - Adverse reactions section (final)
  - Clinical studies section (final)
  - Warnings and Precautions, Contraindications and Boxed Warning sections (draft)
- Examples of labeling in the new format for fictitious drugs
- Information sheets for healthcare professionals and consumers